Answer 1:

Bibliographic Information

Nordihydroguaiaretic acid inhibits insulin-like growth factor signaling, growth, and survival in human neuroblastoma cells. Meyer, Gary E.; Chesler, Louis; Liu, Dandan; Gable, Karissa; Maddux, Betty A.; Goldenberg, David D.; Youngren, Jack F.; Goldfine, Ira D.; Weiss, William A.; Matthay, Katherine K.; Rosenthal, Stephen M. Department of Pediatrics, University of California, San Francisco, CA, USA. Journal of Cellular Biochemistry (2007), 102(6), 1529-1541. Publisher: Wiley-Liss, Inc., CODEN: JCEBD5 ISSN: 0730-2312. Journal written in English. CAN 148:92533 AN 2007:1431613 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Neuroblastoma is a common pediatric malignancy that metastasizes to the liver, bone, and other organs. Children with metastatic disease have a less than 50% chance of survival with current treatments. Insulin-like growth factors (IGFs) stimulate neuroblastoma growth, survival, and motility, and are expressed by neuroblastoma cells and the tissues they invade. Thus, therapies that disrupt the effects of IGFs on neuroblastoma tumorigenesis may slow disease progression. We show that NVP-AEW541, a specific inhibitor of the IGF-I receptor (IGF-IR), potently inhibits neuroblastoma growth in vitro. Nordihydroguaiaretic acid (NDGA), a phenolic compd. isolated from the creosote bush (Larrea divaricata), has anti-tumor properties against a no. of malignancies, has been shown to inhibit the phosphorylation and activation of the IGF-IR in breast cancer cells, and is currently in Phase I trials for prostate cancer. In the present study in neuroblastoma, NDGA inhibits IGF-I-mediated activation of the IGF-IR and disrupts activation of ERK and Akt signaling pathways induced by IGF-I. NDGA inhibits growth of neuroblastoma cells and induces apoptosis at higher doses, causing IGF-I-resistant activation of caspase-3 and a large increase in the fraction of sub-G0 cells. In addn., NDGA inhibits the growth of xenografted human neuroblastoma tumors in nude mice. These results indicate that NDGA may be useful in the treatment of neuroblastoma and may function in part via disruption of IGF-IR signaling.

Answer 2:

Bibliographic Information

The anticancer activity of the transcription inhibitor terameprocol (meso-tetra-O-methyl nordihydroguaiaretic acid) formulated for systemic administration. Lopez, Rocio A.; Goodman, Amanda B.; Rhodes, Melissa; Blomberg, Jessica A. L.; Heller, Jonathan. Erimos Pharmaceuticals, Raleigh, NC, USA. Anti-Cancer Drugs (2007), 18(8), 933-939. Publisher: Lippincott Williams & Wilkins, CODEN: ANTDEV ISSN: 0959-4973. Journal written in English. CAN 147:397981 AN 2007:833453 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Terameprocol (meso-tetra-O-Me nordihydroguaiaretic acid, formerly known as EM-1421 and M4N) is a semi-synthetic small mol. with antitumor activity occurring via selective targeting of Sp1-regulated proteins, including survivin and cdc2 that control cell cycle and apoptosis. Terameprocol is in clin. development as a site-specific transcription inhibitor in solid refractory tumors. The present studies were designed to investigate the in-vitro and in-vivo anticancer activity of terameprocol in a novel hydroxypropyl β-cyclodextrin and polyethylene glycol solvent formulation (designated CPE) designed for safe parenteral administration. Terameprocol powder was dissolved in CPE (20% hydroxypropyl β-cyclodextrin and 50% polyethylene glycol 300 or 30% hydroxypropyl β-cyclodextrin and 25% polyethylene glycol 300) or DMSO and used for in-vitro cell proliferation assays, and in human carcinoma xenograft studies using female athymic nude mice injected with SW-780 human bladder cells. Terameprocol (50 and 100 mg/kg), paclitaxel (5 mg/kg), terameprocol and paclitaxel or vehicle was administered i.p. daily for 21 days. Stock solns. of the CPE formulation were stable for up to 12 mo. Terameprocol CPE formulation showed concn.-dependent inhibition of HeLa and C33A cell proliferation, and was less toxic than terameprocol DMSO formulation. The terameprocol CPE formulation showed no overt toxicities in tumor-bearing mice. Terameprocol alone reduced the rate of tumor growth, and a combination of terameprocol/paclitaxel reduced both the rate and extent of tumor growth. These preclin. results confirm the tumoricidal activity of terameprocol formulated in a solvent suitable for parenteral administration and suggest that terameprocol has improved efficacy when coadministered with paclitaxel.

Answer 3:

Bibliographic Information

Enhancing Engraftment of Neonatal Porcine Xenoislet With CTLA4Ig and Nordihydroguaiaretic Acid. Fu, S.-H.; Chen, Y.-T.; Chiang, C.-H.; Hsu, B. R.-S. Division of Endocrinology and Metabolism, Department of Internal Medicine, Chang-Gung Memorial Hospital, Taoyuan Hsien, Taiwan. Transplantation Proceedings (2006), 38(10), 3283-3285. Publisher: Elsevier Inc., CODEN: TRPPA8 ISSN: 0041-1345. Journal written in English. CAN 146:220518 AN 2006:1328252 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study examd. the combinatory effect on graft survival of neonatal pig pancreatic cell clusters (NPCC) with nordihydroguaiaretic acid (NDGA), a 5-lipoxygenase inhibitor, with systemic CTLA4Ig expression, with local CTLA4Ig and with interleukin-1 (IL-1) receptor antagonist (IL-1ra) expression using a pig to mouse model. About 2000 NPCCs, which were infected with both adenoviruses carrying CTLA4Ig and IL1-1ra genes (each 500 pfu/NPCC), were transplanted beneath the kidney capsule of diabetic BALB/c mice. Two days before transplantation, the recipient mice were either injected with (group C, n = 4; group D, n = 6) or without (group A, n = 7; group B, n = 9) 1 × 1013 pfu/kg body wt. of adenovirus carrying the CTLA4Ig gene. Mice in groups B and D received daily injections of NDGA (20 mg/kg body wt.) s.c. for 4 wk. Blood glucose levels less than 200 mg/dL were defined to be normoglycemic and the transplant termed as a functioning graft for the purpose of calcg. mean graft function time (MFT). Four weeks posttransplantation, an i.p. glucose tolerance test (IPGTT) was performed to calc. the area under the curve (AUC). Blood glucose levels in groups C and D were significantly lower than groups A and B at 1, 2, and 3 wk after transplantation. Graft MFT and AUC of IPGTT in group D were significantly different from those in groups A and B. Our data suggested that a high dosage of systemic expression of CTLA4Ig was effective to enhance xenograft survival and that in it was reinforced by a combination with the macrophage inhibitor NDGA.

Answer 4:

Bibliographic Information

Reversal of multidrug resistance by two nordihydroguaiaretic acid derivatives, M4N and maltose-M3N, and their use in combination with doxorubicin or paclitaxel. Chang, Chih-Chuan; Liang, Yu-Chuan; Klutz, Athena; Hsu, Chuan-I.; Lin, Chien-Fu; Mold, David E.; Chou, Ting-Chao; Lee, Yuan Chuan; Huang, Ru Chih C. Department of Biology, Johns Hopkins University, Baltimore, MD, USA. Cancer Chemotherapy and Pharmacology (2006), 58(5), 640-653. Publisher: Springer, CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 146:372014 AN 2006:760533 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose: Multidrug resistance (MDR) continues to be a major obstacle for successful anticancer therapy. One of the principal factors implicated in MDR is the over expression of P-glycoprotein (Pgp), the product of the MDR1 gene. Methods: Here we explore the possibility of using the transcription inhibitor tetra-O-Me nordihydroguaiaretic acid (M4N) to inhibit Sp1-regulated MDR1 gene expression and restore doxorubicin and paclitaxel sensitivity to multidrug resistant human cancer cells in vitro and in vivo. Results: We found that M4N acted synergistically with doxorubicin and paclitaxel in inhibiting the growth of the cells in culture allowing significant dose redns. of both drugs. We obsd. no such synergism when M4N was used in combination with cisplatin, another chemotherapeutic agent, but not a Pgp substrate, as analyzed by the combination index and isobologram methods. Anal. of MDR1 mRNA and Pgp levels revealed that at sublethal doses, M4N inhibited MDR1 gene expression in the multidrug resistant NCI/ADR-RES cells and reversed the MDR phenotype as measured by Rhodamine-123 retention. In addn., M4N was found to inhibit doxorubicin-induced MDR1 gene expression in drug sensitive MCF-7 breast cancer cells. Conclusions: M4N and maltose-tri-O-Me nordihydroguaiaretic acid (maltose-M3N), a water-sol. deriv. of NDGA, were also able to reverse the MDR phenotype of the tumor cells in a xenograft model system and combination therapy with M4N or maltose-M3N and paclitaxel was effective at inhibiting growth of these tumors in nude mice.

Answer 5:

Bibliographic Information

Systemic Treatment with Tetra-O-Methyl Nordihydroguaiaretic Acid Suppresses the Growth of Human Xenograft Tumors. Park, Richard; Chang, Chih-Chuan; Liang, Yu-Chuan; Chung, Yousun; Henry, Ryan A.; Lin, Elaine; Mold, David E.; Huang, Ru Chih C. Department of Biology, Johns Hopkins University, Baltimore, MD, USA. Clinical Cancer Research (2005), 11(12), 4601-4609. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 143:318499 AN 2005:513725 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose: We have previously shown that the transcriptional inhibitor tetra-O-Me nordihydroguaiaretic acid (M4N) induces growth arrest in tumor cells and exhibits tumoricidal activity when injected intratumorally into tumor cell explants in mice. The expts. reported here were designed to det. whether M4N can be given systemically and inhibit the growth of five different human xenograft tumors. Exptl. Design: Nude (nu/nu) mice bearing xenografts of each of five human tumor types (i.e., hepatocellular carcinoma, Hep 3B; prostate carcinoma, LNCaP; colorectal carcinoma, HT-29; breast carcinoma, MCF7; and erythroleukemia, K-562) were treated with M4N given i.v. or i.p. in a Cremophor EL-based solvent system or orally in a corn oil based diet. Tumors from the treated animals were measured weekly and analyzed for the expression of the Cdc2 and survivin genes, both previously shown to be down-regulated by M4N. Results: Systemic M4N treatment suppressed the in vivo growth of xenografts in each of the five human tumor types. Four of the five tumor models were particularly sensitive to M4N with tumor growth inhibitions (T/C values) of ≤42%, whereas the fifth, HT-29, responded to a lesser extent (48.3%). Growth arrest and apoptosis in both the xenograft tumors and in the tumor cells grown in culture were accompanied by redns. in both Cdc2 and tumor-specific survivin gene expression. Pharmacokinetic anal. following oral and i.v. administration to ICR mice indicated an abs. bioavailability for oral M4N of .apprx.88%. Minimal drug-related toxicity was obsd. Conclusion: These preclin. studies establish that when given systemically, M4N can safely and effectively inhibit the growth of human tumors in nude mice.

Answer 6:

Bibliographic Information

Effects of NDGA on the growth of a human malignant glioma cell line CHG-5. Xu, Chengping; Bian, Xiuwu; Zhang, Rong; Yin, Yusong. Southwest Hospital, Third Military Medical University, Chongqing, Peop. Rep. China. Di-San Junyi Daxue Xuebao (2004), 26(8), 670-673. Publisher: Di-San Junyi Daxue Xuebao Bianjibu, CODEN: DYXUE8 ISSN: 1000-5404. Journal written in Chinese. CAN 142:211658 AN 2004:967100 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Colorimetric MTT assay, flow cytometry, and light microscopy were used to investigate the proliferation in vitro, cell cycles, apoptosis of CHG-5 cells, and the growth of xenografted tumor in nude mice. Nordihydroguaiaretic acid (NDGA) significantly inhibited the proliferation of CHG-5 cells in vitro. The cells in G0/G1 phase increased, but the cells in S, G2/M phases decreased, and apoptotic cells increased significantly. After treatment of NDGA (50 mg/kg, i.p.) 5 d after the inoculation of tumor cells, the xenografted tumor vol. reduced remarkably without significantly toxic and side effects. The inhibitory effect of NDGA on the growth of CHG-5 cells may be correlated with the regulation of cell cycles and induction of apoptosis.

Answer 7:

Bibliographic Information

Lipoxygenase inhibitors attenuate growth of human pancreatic cancer xenografts and induce apoptosis through the mitochondrial pathway. Tong, Wei-Gang; Ding, Xian-Zhong; Witt, Richard C.; Adrian, Thomas E. Gastrointestinal Oncology Laboratories, Department of Surgery, Northwestern University Medical School, Chicago, IL, USA. Molecular Cancer Therapeutics (2002), 1(11), 929-935. Publisher: American Association for Cancer Research, CODEN: MCTOCF ISSN: 1535-7163. Journal

written in English. CAN 139:17258 AN 2003:69743 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Several studies have suggested that high dietary fat intake, particularly essential fatty acids, is assocd. with pancreatic cancer development and growth. Our previous studies have demonstrated that blockade of either the 5-lipoxygenase (LOX) or 12-LOX pathway of arachidonic acid metab. inhibited pancreatic cancer cell proliferation and induced apoptosis. This study investigated the underlying mechanisms for LOX inhibitor-induced apoptosis and the potential of LOX inhibitors as antipancreatic cancer agents using the athymic mice xenograft model. Apoptosis of pancreatic cancer cells induced by LOX inhibitors (including the nonselective LOX inhibitor nordihydroguaiaretic acid, the 5-LOX inhibitor Rev-5901, and the 12-LOX inhibitor baicalein) was confirmed by growth inhibition, annexin V binding, and terminal deoxynucleotidyl transferase-mediated nick end labeling assay in MiaPaCa-2 and AsPC-1 human pancreatic cancer cells. Expression of the antiapoptotic proteins Bcl-2 and Mcl-1 was significantly decreased after LOX inhibitor treatment while that of the proapoptotic protein bax was increased. LOX inhibitors also markedly induced the release of cytochrome c from mitochondria into the cytosol. Caspase-9, caspase-7, and caspase-3 but not caspase-8 were activated after treatment, concomitant with cleavage of the caspase-3 substrate poly(ADP-ribose) polymerase. In vivo studies in the athymic mice xenograft model also confirmed the growth inhibitory effect and induction of apoptosis by these LOX inhibitors in pancreatic cancer. In conclusion, LOX inhibitors block pancreatic cancer cell proliferation and induce apoptosis through the mitochondrial pathway both in vivo and in vitro. LOX inhibitors are likely to be valuable for the treatment of human pancreatic cancer.

Answer 8:

Bibliographic Information

Effects of nordihydroguaiaretic acid on xenograft of human malignant glioma cells in nude mice. Guo, Deyu; Chen, Yisheng; Du, Linlin; Bian, Xiuwu. Dep. Pathology, Third Military Medical Univ., Chungking, Peop. Rep. China. Di-San Junyi Daxue Xuebao (1999), 21(10), 702-704. Publisher: Di-San Junyi Daxue, CODEN: DYXUE8 ISSN: 1000-5404. Journal written in Chinese. CAN 132:245956 AN 1999:815508 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of nordihydroguaiaretic acid (NDGA) on the xenograft of human malignant glioma cells was studied in nude mice. NDGA inhibited the growth of the xenograft of human malignant glioma cell line SHG-44 in nude mice. NDGA induced the differentiation of the xenograft cells and blocked the cell growth cycle in the G1 $\rightarrow$ S phase. Thus, the therapeutic effects of NDGA on human malignant glioma in vivo are similar to those in vitro.

Answer 9:

Bibliographic Information

The effect of glucose administration on the uptake of Photofrin II in a human tumor xenograft. Peng, Q.; Moan, J.; Cheng, L. S. Dep. Biophys., Inst. Cancer Res., Oslo, Norway. Cancer Letters (Shannon, Ireland) (1991), 58(1-2), 29-35. CODEN: CALEDQ ISSN: 0304-3835. Journal written in English. CAN 115:67635 AN 1991:467635 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Athymic BALB/c nude mice bearing a human melanoma cell line LOX were given the photosensitizing drug Photofrin II (10 mg/kg) i.p. Mice were also given i.p. glucose, galactose, or glucose plus nordihydroguaiaretic acid (NDGA, an inhibitor of glycolysis). Multiple injections of glucose (3 g/kg) given at -1, 0, +1, and +3 h relative to the injection of Photofrin II at time 0 increased the uptake of Photofrin II in the tumor 4 h after the Photofrin II injection, while the uptake in the other tissue remained unchanged. Galactose had no effect on the uptake of Photofrin II in the tissues studied (tumor, muscle, skin, and liver). NDGA abolished the effect of glucose.

Answer 10:

Bibliographic Information

Unique proteomic features induced by a potential antiglioma agent, Nordy (dl-nordihydroguaiaretic acid), in glioma cells. Bian Xiu-Wu; Xu Jian-Ping; Ping Yi-Fang; Wang Yan; Chen Jian-Hong; Xu Cheng-Ping; Wu Yu-Zhang; Wu Jun; Zhou Xiang-Dong; Chen Yi-Sheng; Shi Jing-Quan; Wang Ji Ming Institute of Pathology, Southwest Hospital, Third Military Medical University, Chongqing, China. bianxiuwu@263.net Proteomics (2008), 8(3), 484-94. Journal code: 101092707. ISSN:1615-9853. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 18232056 AN 2008221223 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Nordy is a chirally synthesized compound of a natural lipoxygenase inhibitor nordihydroguaiaretic acid. In this study, we found that Nordy inhibited the growth of human glioma cell lines in vitro and their tumorigenicity in mice. In addition, Nordy promoted differentiation of highly malignant human glioma cells. Investigation into the mechanistic basis of Nordy activities revealed that it altered the pattern of protein expression profiles in tumor cells. By using 2-DE, we found that in human glioma cell lines, at least six proteins were down-regulated after Nordy treatment, while four proteins were elevated in the same cells. Among the six down-regulated proteins, microsequencing with MALDI TOF MS confirmed the identity of five: proliferation-associated gene A (PAG-A), alternative splicing factor-3 (ASF-3), beta-galactoside binding lectin, eukaryotic translation initiation factor 5A (eIF-5A), and coffilin-1 (nonmuscle). Four up-regulated proteins were GST-pi, glyceraldehyde-3-phosphate dehydrogenase, alpha-enolase, and cyclophilin. All these proteins have been reported to participate in key cellular functions including proliferation, metabolism, differentiation, apoptosis, and gene transcription. Our results suggest that Nordy may constitute a promising drug lead for the development of novel antitumor agents targeting proteins that control tumor cell function at multiple levels.

Answer 11:

Bibliographic Information

A novel lipoxygenase inhibitor Nordy attenuates malignant human glioma cell responses to chemotactic and growth stimulating factors. Chen Jian-hong; Yao Xiao-hong; Gong Wanghua; Hu Jinyue; Zhou Xiang-dong; Chen Keqiang; Liu Hong; Ping Yi-fang; Wang Ji Ming; Bian Xiu-wu Institute of Pathology, Southwest Hospital, Third Military Medical University, Chongqing, 400038, China Journal of neuro-oncology (2007), 84(3), 223-31. Journal code: 8309335. ISSN:0167-594X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, N.I.H., EXTRAMURAL); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 17377739 AN 2007415644 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Nordy is a chiral compound synthesized based on the structure of a natural lipoxygenase (LO) inhibitor nordihydroguaiaretic acid (NDGA) from plants. The aim of the present study is to investigate the effect of Nordy on malignant human glioma cell responses to chemoattractants and growth promoting signals. We found that Nordy, in a non-cytotoxic concentration range, potently inhibited the chemotaxis and calcium flux of a human glioblastoma cell line U87 induced by a formylpeptide receptor (FPR) agonist, formyl-methionyl-leucyl-phenylalanine (fMLF) and epidermal growth factor (EGF). U87 cells treated by Nordy also showed a significantly impaired proliferation and expression of mRNA for vascular endothelial growth factor (VEGF) induced by fMLF. The chemotactic and proliferation responses of Nordy treated U87 cells to EGF were concomitantly diminished. Further experiments revealed that Nordy did not significantly affect FPR gene expression in U87 cells, but attenuated the activation of a plethora of signaling molecules including ERK1/2, p38, JNK, and Akt when the cells were stimulated by fMLF. EGF-induced EGF receptor phosphorylation was also inhibited in Nordy-treated U87 cells. Moreover, Nordy significantly reduced the tumorigenicity of U87 cells in nude mice. Our results suggest that Nordy is capable of inhibiting glioma cell responses to signals that

promote cell motility, growth and production of VEGF. Thus, Nordy may constitute a molecular basis for the development of novel anti-cancer drugs.

Answer 12:

Bibliographic Information

Mechanisms of nordihydroguaiaretic acid-induced growth inhibition and apoptosis in human cancer cells. Seufferlein T; Seckl M J; Schwarz E; Beil M; v Wichert G; Baust H; Luhrs H; Schmid R M; Adler G Department of Internal Medicine I, University of Ulm, D-89081 Ulm, Germany. thomas.seufferlein@medizin.uni-ulm.de British journal of cancer (2002), 86(7), 1188-96. Journal code: 0370635. ISSN:0007-0920. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 11953870 AN 2002216653 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Lipoxygenase metabolites of arachidonic acid can act as growth promoting factors for various cancer cell lines. Here we demonstrate that the 5-lipoxygenase inhibitor nordihydroguaiaretic acid potently inhibits anchorage-independent growth of human pancreatic and cervical cancer cells in soft agar and delays growth of pancreatic and cervical tumours established in athymic mice. Furthermore, nordihydroguaiaretic acid induces apoptosis of these cancer cells in vitro and in vivo. Potential mechanisms mediating these effects of nordihydroguaiaretic acid were examined. Nordihydroguaiaretic acid had no inhibitory effect on growth and survival signals such as tyrosine phosphorylation of the epidermal growth factor receptor or basal and growth factor-stimulated activities of extracellular signal-regulated kinase 1/2, p70(s6k) and AKT but selectively inhibited expression of cyclin D1 in the cancer cells. In addition, treatment with nordihydroguaiaretic acid lead to a disruption of the filamentous actin cytoskeleton in human pancreatic and cervical cancer cells which was accompanied by the activation of Jun-NH(2)-terminal kinase and p38(mapk). Similar effects were obtained by treatment of the cancer cells with cytochalasin D. These results suggest that nordihydroguaiaretic acid induces anoikis-like apoptosis as a result of disruption of the actin cytoskeleton in association with the activation of stress activated protein kinases. In conclusion, nordihydroguaiaretic acid could constitute a lead compound in the development of novel therapeutic agents for various types of cancer.

Answer 13:

Bibliographic Information

tetra-O-methylnordihydroguaiaretic acid inhibits melanoma in vivo. Lambert J D; Meyers R O; Timmermann B N; Dorr R T Arizona Cancer Center, The University of Arizona, P.O. Box 245024, 1515 North Campbell Avenue, Tucson, AZ 85724-5024, USA Cancer letters (2001), 171(1), 47-56. Journal code: 7600053. ISSN:0304-3835. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 11485827 AN 2001439930 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

tetra-O-methylnordihydroguaiaretic acid is a derivative of a naturally-occurring lignan, nordihydroguaiaretic acid, that has previously been shown to inhibit various cancer types in vitro and in vivo. Additionally, nordihydroguaiaretic acid has been shown to have nephrotoxic effects in the rat. Here we show that tetra-O-methylnordihydroguaiaretic acid inhibits the growth of a number of tumor cell lines in vitro by inducing apoptosis in a non-schedule-dependent manner. Further, this compound inhibits the synthesis of DNA by melanoma cells and causes cell cycle arrest in G0/G1 and G2/M phases of the cell cycle. tetra-O-Methylnordihydroguaiaretic acid also inhibits the growth of both murine and human melanomas and human colon cancer in vivo without apparent hepatic or renal toxicity.

Answer 14:

Bibliographic Information

Lipoxygenase inhibitors prevent lung carcinogenesis and inhibit non-small cell lung cancer growth. Moody T W; Leyton J; Martinez A; Hong S; Malkinson A; Mulshine J L Cell and Cancer Biology Department, National Cancer Institute, Rockville, Maryland, USA. moodyt@bprb.nci.nih.gov Experimental lung research (1998), 24(4), 617-28. Journal code: 8004944. ISSN:0190-2148. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 9659587 AN 1998323772 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The effects of lipoxygenase inhibitors were investigated using human lung cancer cell lines and A/J mice. By RT-PCR, 5-, 12-, and 15-lipoxygenase mRNA was detected in NSCLC cells. NDGA inhibited 5-LO activity in adenocarcinoma cell line NCI-H1264. Using an MTT assay, NDGA, MK591 and AA861 inhibited the growth of NSCLC cell lines tested with IC50 values of 3, 2, and 7 microM, respectively. Using a clonogenic assay, 10 microM NDGA significantly reduced NSCLC colony number. NDGA significantly slowed NSCLC xenograft growth in nude mice. When the tumors were excised and analyzed, nude mice treated with NDGA had significantly more apoptotic figures than did untreated tumors. A/J mice treated with urethane developed adenomas after 4 months and NDGA administration significantly reduced lung adenoma number. These data indicate that lipoxygenase inhibitors inhibit lung cancer growth and prevent lung carcinogenesis.